

The candidate histocompatibility locus of a Basal chordate encodes two highly polymorphic proteins.

Journal: PLoS One

Publication Year: 2013

Authors: Marie L Nydam, Nikolai Netuschil, Erin Sanders, Adam Langenbacher, Daniel D Lewis, Daryl A Taketa, Arumugapradeep Marimuthu, Andrew Y Gracey, Anthony W De Tomaso

PubMed link: 23826085

Funding Grants: Curriculum Development and Implementation of Stem Cell Technology and Laboratory Management Emphasis in an Established MS Biotechnology and Bioinformatics Program at California State University Channel Islands and Co-development of a GE Course on Stem Cel

Public Summary:

The basal chordate *Botryllus schlosseri* undergoes a natural transplantation reaction governed by a single, highly polymorphic locus called the *fuhc*. Our initial characterization of this locus suggested it encoded a single gene alternatively spliced into two transcripts: a 555 amino acid-secreted form containing the first half of the gene, and a full-length, 1008 amino acid transmembrane form, with polymorphisms throughout the ectodomain determining outcome. We have now found that the locus encodes two highly polymorphic genes which are separated by a 227 bp intergenic region: first, the secreted form as previously described, and a second gene encoding a 531 amino acid membrane-bound gene containing three extracellular immunoglobulin domains. While northern blotting revealed only these two mRNAs, both PCR and mRNA-seq detect a single capped and polyadenylated transcript that encodes processed forms of both genes linked by the intergenic region, as well as other transcripts in which exons of the two genes are spliced together. These results might suggest that the two genes are expressed as an operon, during which both genes are co-transcribed and then trans-spliced into two separate messages. This type of transcriptional regulation has been described in tunicates previously; however, the membrane-bound gene does not encode a typical Splice Leader (SL) sequence at the 5' terminus that usually accompanies trans-splicing. Thus, the presence of stable transcripts encoding both genes may suggest a novel mechanism of regulation, or conversely may be rare but stable transcripts in which the two mRNAs are linked due to a small amount of read-through by RNA polymerase. Both genes are highly polymorphic and co-expressed on tissues involved in histocompatibility. In addition, polymorphisms on both genes correlate with outcome, although we have found a case in which it appears that the secreted form may be major allorecognition determinant.

Scientific Abstract:

The basal chordate *Botryllus schlosseri* undergoes a natural transplantation reaction governed by a single, highly polymorphic locus called the *fuhc*. Our initial characterization of this locus suggested it encoded a single gene alternatively spliced into two transcripts: a 555 amino acid-secreted form containing the first half of the gene, and a full-length, 1008 amino acid transmembrane form, with polymorphisms throughout the ectodomain determining outcome. We have now found that the locus encodes two highly polymorphic genes which are separated by a 227 bp intergenic region: first, the secreted form as previously described, and a second gene encoding a 531 amino acid membrane-bound gene containing three extracellular immunoglobulin domains. While northern blotting revealed only these two mRNAs, both PCR and mRNA-seq detect a single capped and polyadenylated transcript that encodes processed forms of both genes linked by the intergenic region, as well as other transcripts in which exons of the two genes are spliced together. These results might suggest that the two genes are expressed as an operon, during which both genes are co-transcribed and then trans-spliced into two separate messages. This type of transcriptional regulation has been described in tunicates previously; however, the membrane-bound gene does not encode a typical Splice Leader (SL) sequence at the 5' terminus that usually accompanies trans-splicing. Thus, the presence of stable transcripts encoding both genes may suggest a novel mechanism of regulation, or conversely may be rare but stable transcripts in which the two mRNAs are linked due to a small amount of read-through by RNA polymerase. Both genes are highly polymorphic and co-expressed on tissues involved in histocompatibility. In addition, polymorphisms on both genes correlate with outcome, although we have found a case in which it appears that the secreted form may be major allorecognition determinant.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/candidate-histocompatibility-locus-basal-chordate-encodes-two-highly>